

Application Serial No. 10/005,465
Office Action dated May 19, 2003
Reply dated August 19, 2003

AMENDMENTS TO THE SPECIFICATION

Please delete the paragraph beginning at page 3, line 25, which starts with "FIGURE 2 depicts..."

Please delete the paragraph beginning at page 4, line 4, which starts with "FIGURE 3 depicts..."

Please delete the paragraph beginning at page 4, line 12, which starts with "FIGURE 4 depicts..."

Please add the following new paragraph after page 8, line 25:

The retinal thickness (edema) at day 1 post laser treatment (photocoagulation) in rats was determined. The retinal thickness was measured from eyes of rats treated with TRIEN or TETREN or D-PA, and compared to the retinal thickness from eyes of rats injected with saline (controls) and to normal retina (no laser treatment and no drug/saline injections). Coherent Argon Dye Laser irradiation at 545 nm wavelength was delivered through a slit lamp. A total of 6 laser spots were placed separately using a setting of 50 um diameter, 0.1 sec duration and 150 mW intensity. The retinal thickness of eyes from control animals (saline injected) is greater than that of normal (no laser treatment, no drug/saline injections) retina and eyes from animals treated with TRIEN or TETREN. The retinal thickness of eyes from animals injected with D-PA is greater than that in control eyes.

Please replace the paragraph beginning at page 8, line 26, with the following amended paragraph:

A comparison was made of rat eyes following photocoagulation therapy, where the rats received either TRIEN, TETREN, D-PA or no copper chelator (control treated) prior to laser therapy. When the rat eyes were compared on the basis of retinal thickness, the eyes from control animals (saline injected) were greater than those of the TRIEN or TETREN groups as represented in Figure 2. At twenty-four hours post photocoagulation treatment, the retinal thickness of eyes from control animals

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was 50% greater than that in normal retina, where no laser treatment and no copper chelator was given. The retinal thickness of eyes of TRIEN injected animals was 23% greater than that in normal retina and the retinal thickness of eyes from TETREN-treated animals was 26% greater than that in normal retina. However, when the retinal thickness of eyes from D-PA treated animals was ~~measure~~ measured they were found to be 85% greater than that of normal retinal thickness and 35% greater than that in the control animals.

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Please add the following new paragraph before the paragraph beginning at page 9, line 6:

The retinal thickness (edema) at day 1 post PDT in rabbits was also determined. Retinal edema at 1 day post PDT was measured from animals treated with TRIEN or TETREN (0.2mM/day), or from control animals (saline injected). Laser light at 689 nm at a power of 600 mW/cm² was delivered on a 5 mm spot in one eye from a diode laser (Coherent) using a slit lamp delivery system 15 minutes after verteporfin infusion. The retinal thickness from animals treated with TRIEN and TETREN is significantly less than that in control (saline injected) animals.

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Please replace the paragraph beginning at page 9, line 6, with the following amended paragraph:

A comparison was also made of rabbit eyes following PDT, where the rabbits received either TRIEN, TETREN or no copper chelator (control treated) prior to laser therapy. When the rabbit eyes were compared on the basis of retinal thickness, the eyes from control treated animals(saline injected) were greater than that eyes from animals treated with TRIEN or TETREN or untreated eyes, ~~as shown in Figure 3~~. Twenty-four hours after PDT treatment, the retinal thickness of eyes from control animals (saline injected) was 140% greater than that in normal retina; the retinal thickness of TRIEN treated eyes was 50% greater than that in normal retina; the retinal thickness of TETREN treated eyes was 45% greater than that in normal retina.

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Please add the following new paragraph after page 9, line 20:

The ED-1 immunostaining of retina at Day 1 post photocoagulation treatment in rats was measured and the number of ED-1 immunoreactive cells determined. ED-1 is a marker for macrophage cells. Coherent Argon Dye Laser irradiation at 545 nm wavelength was delivered through a slit lamp using a setting of 50 um diameter, 0.1 sec duration and 150 mW intensity. The lesions were quantified by counting the number of positive cells in an average of four 40x objective fields. The numbers of ED-1 positive cells were less in retina of TRIEN or TETREN treated animals compared to control (saline injected) animals. The numbers of ED-1 positive cells of Trientine-treated eyes were two times less than of control. The numbers of ED-1 positive cells of TETREN treated eyes were 2.5 times less than that of control animals.

Please replace the paragraph beginning at page 9, line 21, with the following amended paragraph:

To determine if the tissue inflammation could be correlated with the immune response were stained with macrophage antibody (ED-1). TRIEN and TETREN inhibited the immunoresponse in ocular tissues following laser therapy. All experimental animals showed a similar sequence of immunohistochemical findings, ~~which are summarized in Figure 4~~. At twenty-four hours after laser treatment, the macrophage staining was clearly evident in eyes from control animals (saline injected). In eyes from TRIEN and TETREN treated animals showed fewer macrophages at the laser therapy sites. The number of ED-1 positive retina cells in TRIEN treated animals were approximately half that of the controls (saline injected). And similarly the number of ED-1 positive retina cells in TETREN treated animals were more than half that of control animals.